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LIVER

Benzyl alcohol limits acute liver injury

Paracetamol (acetaminophen) overdose is one of the most common causes of acute liver injury worldwide. Treatment options are currently limited to *N*-acetylcysteine administration or liver transplantation, but a study published in *Hepatology* has identified benzyl alcohol as a potential new therapy. The study demonstrated that mice receiving paracetamol with benzyl alcohol had considerably less liver injury than the control group receiving paracetamol alone.

Paracetamol overdose results in activation of innate immune signalling pathways, leading to increased inflammatory cytokine and chemokine production and cellular injury. Mice treated with benzyl alcohol had reduced levels of cytokines and chemokines compared with controls.

Most notably, Toll-like receptor (Tlr) 9, receptor for advanced glycosylation end products, Nalp3 inflammasome, caspase-1 and high mobility group protein B1 signalling were involved in paracetamol-mediated liver injury. As these pathways involve Tlr4 activation, the authors investigated Tlr4 as the primary route of hepatoprotection conferred by benzyl alcohol.

Global *Tlr4*-knockout mice received no benefit from benzyl alcohol after paracetamol exposure, indicating that this receptor was in part responsible for the protection of the liver observed in wild-type mice. Cell-type-specific *Tlr4* knockdown further identified that hepatoprotection was dependent upon signalling specifically in myeloid cells.

The authors hypothesize that benzyl alcohol activation of Tlr4 in mice prevents the amplification of liver injury by molecules that perpetuate immune responses and negatively regulates activated immune pathways. Future studies will focus on developing benzyl alcohol as a therapy.

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Original article Cai, C. *et al.* Benzyl alcohol attenuates acetaminophen-induced acute liver injury in a toll-like receptor-4 dependent pattern in mice. *Hepatology* doi:10.1002/hep.27201